

REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-25, 27-41 and 43-51 are currently pending (contrary to the listing in the Office Action which lists claim 42 as withdrawn, this claim was canceled in the last amendment), with claims 1-24 and 28-36 withdrawn from consideration as directed to non-elected inventions. Upon entry of this amendment, claims 50 and 51 are amended and claims 1-24, and 28-36 canceled without prejudice or disclaimer. Applicants reserve the right to reintroduce the unamended or canceled claims in this or another application. New claim 52 is introduced upon entry of this amendment. Claims 25, 27, 37-41 and 43-52 are thus pending following entry of this amendment.

New claim 52 is supported throughout the specification, including, for example, at page 33, line 29 to page 35, line 33.

II. Drawings

The Office Action states that only informal drawings have been filed and that formal drawings will be required once the application is allowed. It is noted that formal drawings were submitted with the amendment that was filed on November 26, 2002. Another set of these figures are attached in case the set submitted earlier cannot be located.

III. Information Disclosure Statement

The Office Action states that the supplemental information disclosure statement submission on April 18, 2003 has not been considered because the U.S. application listed in the IDS was not listed on PTO form 1449. This issue is rendered moot because, as described below with respect to the double patenting rejection, the U.S. application listed in this IDS (U.S. Application No. 09/686,019) has been abandoned; this was the only document cited in that particular IDS.

IV. Claim Rejections under 35 U.S.C. §112, First Paragraph

Claims 25, 27, 37-41 and 43-51 are rejected under 35 U.S.C. 112, first paragraph because these claims are said to encompass subject matter that has not been described with sufficient detail to enable one of ordinary skill to make or use the invention without undue experimentation. It is specifically asserted that it would require undue experimentation to prepare the CCX CKR polypeptides that are recited in the current claims and identify those with the recited activity without undue experimentation. As described in greater detail below, Applicants respectfully disagree for at least the following two general reasons: (i) the Office is applying an incorrect enablement standard, and (ii) the rationale presented in the Office Action is inconsistent with statements in Guidelines promulgated by the Office.

The primary reason the Office Action gives for concluding that the current claims lack enablement is because of the difficulty in *predicting* function based upon sequence. For example, the Office Action states on page 5, lines 15-16, that the "problem of *predicting* protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex." In fact, the issues concerning difficulties in *predicting* function from sequence is raised repeatedly throughout the Office Action (see, e.g., page 7, line 14; page 8, lines 2 and 10; and page 9, line 4). Thus the Office Action implies that the specification fails to enable the polypeptides that are recited in the current claims, unless the disclosure enables of ordinary skill to *predict* which polypeptides would have the recited chemokine binding activity.

This, however, is not the appropriate standard. As pointed out in the last response, when evaluating enablement:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, *if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. (In re Wands, 8 USPQ2d, 1400, 858 F.2d 731 (Fed. Cir. 1988), emphasis added).*

Thus, based upon this holding by the Federal Circuit, experimentation is not deemed to be undue if EITHER of two requirements are satisfied: (1) the experimentation is routine, OR (2) the specification provides reasonable guidance in the direction the experimentation should proceed. Although only *one* of these criteria need be satisfied, it is submitted that the specification satisfies *both*.

With respect to the first criterion, the issue thus is whether one of ordinary skill in the art can routinely (a) make a polypeptide that is a fragment or variant of SEQ ID NO:2, wherein the variant has 90% sequence identity to SEQ ID NO:2 and (b) determine whether such a fragment or variant has the recited chemokine binding activity. It is submitted that the answer to both of these inquiries is "yes."

With respect to issue (a), a copy of a section from the well-known 1989 Creighton reference on proteins is enclosed. This section states that "[p]resent day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions" ("Protein Structure: A Practical Approach" (Creighton, T.E., Ed.) IRL Press, 1989, pp. 184-185). Since this edition of Creighton significantly predates the priority date of the instant application, those of ordinary skill in the art could have readily made fragments and variants such as recited in the current claims as of the priority date of the application. With respect to issue (b), the specification describes a variety of assays that can be utilized to detect binding between the CCX CKR polypeptides and chemokines that are recited in the present claims (see, e.g., page 17, line 16 to page 18, line 16). Some of the assays described in the section are based upon published assays, and thus are routine in the art. The assays described on page 34, line 13 to page 35, line 23 and in Example 4 can also be utilized with minor modification to detect binding between a test polypeptide and a selected chemokine (e.g., by substituting the test polypeptide for the CCX CKR polypeptide referred to in the specification). Assays such as those described in these sections of the specification were utilized by the inventors to screen over 80 chemokines for their ability to bind CCX CKR polypeptides (see, e.g., Example 5), thus demonstrating the ability of these assays to be utilized in a routine manner as a high throughput screen.

So one of ordinary skill in the art is free to make polypeptides that differ from SEQ ID NO:2 using techniques that Creighton says are routine in the art. The resulting polypeptides can then be analyzed for their ability to bind the recited chemokines using the routine assays described in the specification. This is all that the law requires to satisfy the requirements of criterion (1) listed above. For this reason alone, it is submitted that the current methods are thus enabled.

Nonetheless, it is also submitted that the specification satisfies criterion (2), because the specification provides guidance on the direction that experimentation should proceed. As described in detail in the last response, the specification provides guidance on what amino acid positions could potentially be altered and with what amino acids without unduly affecting activity. The specification, for instance, teaches that variants can involve conservative substitutions (see, e.g., page 7, line 29 to page 8, line 14). The specification goes on to list specific examples of conservative substitutions (see, e.g., paragraph bridging pages 7 and 9) and cites to a 1984 Creighton reference for further guidance on this issue. Moreover, Fig. 2A provides amino acid sequence alignments between CCX CKR and four other chemokine receptors that illustrate conserved and non-conserved regions between these five receptors. Two of these receptors have binding profiles that overlap with CCX CKR. CCR9, for example, binds TECK and CCR7 binds SLC and ELK (see, e.g., page 33, lines 6-27). Thus, those of ordinary skill in the art would know that one logical approach for making variants of SEQ ID NO:2 that have the binding activity recited in the current claims would be to make alterations in non-conserved regions, as such regions appear to tolerate differences.

The Office Action discounts this by stating that these assertions cannot be accepted without supporting evidence. Why the Office considers these statements to lack support is unclear. That the sequences include regions of similarity is clear from Figure 2A. The prior response made clear that the references listed on page 33, lines 6-27 included references that discussed CCR7 and CCR9 binding activity. Nonetheless, copies of the following articles are enclosed to confirm that CCR7 binds ELC and SLC: 1) Yoshida, R. et al. (1998) J. Biol. Chem. 273:7118-7122; and 2) Yoshida R., et al. (1997) J. Biol. Chem. 272:13803-13809. Also enclosed are articles that describe binding between CCR9 and TECK, including: 1) Zaballo et

al. (1999) J. Immunol. 162:5671, and 2) Youn et al. (1999) Blood 94:2533). So in view of the guidance provided on appropriate modifications to the polypeptide sequence, it is submitted for this reason also that the current claims are enabled.

Because the criteria established by the Federal Circuit do not require *predictive* ability to satisfy the enablement requirement, the numerous references cited in the Office Action that are said to support the proposition that it is extremely difficult to *predict* function based upon sequence lack relevance. Moreover, it is noted that at least one of the cited references (Murdoch) discusses chemokine receptors that only have 49% similarity in sequence, whereas the current claims refer to variants that have at least 90% sequence identity. That certain chemokine receptors with relatively low levels of sequence similarity have different activities is of little relevance since the current claims require significantly higher levels of sequence identity.

Apart from the fact that it appears that the Office Action applies the wrong standard for evaluating enablement, the conclusion the Office Action reaches is at odds with the discussion in the "Synopsis of Application of Written Description Guidelines" (Guidelines) that the Patent Office has promulgated. Although the current rejection is an enablement rather than written description rejection, a statement in the Written Description Guidelines is nonetheless pertinent to the current rejection.

As noted in the last response, Example 14 in the Guidelines focuses on a claim that is similar to the pending claims; the claim reads:

"A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A to B."

In the Analysis section of Example 14, it is noted that "procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain activity are conventional in the art." The Office thus takes the view in these Guidelines that those of ordinary skill in the art can make and use polypeptides that: (i) have a relatively high level of sequence identity to a reference sequence, and (ii) share a specific activity. This is the case with the polypeptides recited in the current claims.

As pointed out in previous responses, the Guidelines are also clear that polypeptides defined according to criteria (i) and (ii) satisfy the written description requirement. To satisfy the written description requirement, the specification must describe the claimed invention with sufficient clarity such that one of ordinary skill in the art could conclude that the inventors were in possession of the claimed invention at the time the application was filed (see, e.g., MPEP 2163.02). To do this, the specification must describe the claimed invention such that one of ordinary skill can envision what is encompassed by the claims. It would be inconsistent for the Office to say on one hand that a specification and claim set that satisfies criteria (i) and (ii) allow one of ordinary skill to envision the claimed invention, but then on the other hand to say that such a specification nonetheless fails to satisfy the enablement requirement for failure to describe how to make and use the invention.

V. Double Patenting

Claims 25, 27 and 43-49 are said to be unpatentable under obviousness-type double patenting with respect to claims 25-27 of U.S. Application No. 09/686,019. A restriction requirement was mailed on May 22, 2003 in the 09/686,019 application, with November 22, 2003 thus being the final deadline for filing a response. A response was not filed by this deadline; thus, the application has been allowed to go abandoned. Consequently, this ground of rejection is moot.

If the Examiner believes a telephone conference would expedite prosecution of

Appl. No. 09/721,341
Amdt. dated January 20, 2004
Reply to Office Action of August 20, 2003

PATENT

this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Scott Ausenhus". The signature is fluid and cursive, with the first name "Scott" written in a larger, more prominent script than the last name "Ausenhus".

Scott L. Ausenhus
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Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

By:


Tara N. Damhoff

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

GOSLING et al.

Application No.: 09/721,341

Filed: November 21, 2000

For: METHOD FOR IDENTIFYING A
MODULATOR OF THE BINDING OF
CCX CKR POLYPEPTIDE TO A
CHEMOKINE (AMENDED)

Examiner: Bunner, Bridget E.

Art Unit: 1647

SUPPLEMENTAL INFORMATION
DISCLOSURE STATEMENT UNDER 37
CFR §1.97 and §1.98

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. Copies of the references are enclosed.

It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

This IDS is being filed before the mailing date of the final Office Action or Notice of Allowance.

Please charge the IDS fee of \$180 to Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



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